NCT04011644

Integrating mHealth for alcohol use disorders into clinical practice

07.13.2023

Protocol
HS IRB #2019-0337
Version 5. 10/17/19
Version 6. 04/07/20
Version 7. 10/09/20
Version 8. 01/26/21
Version 9. 08/18/21
Version 10. 07/13/23

Integrating mHealth for alcohol use disorders into clinical practice

PRINCIPAL INVESTIGATOR: **Andrew R. Quanbeck, PhD.**
University of WI – Madison
Department: Family Medicine
800 University Bay Drive
Madison, WI 53705
Phone 608.262.7385
Email: ARQUANBE@WISC.EDU

COORDINATING CENTER: Implementation Science and Engineering Lab

CO-INVESTIGATORS: **Randall Brown, M.D., PhD.**
Department: Family Medicine and Community Health
1100 Delaplaine Ct Room 3832
Madison, WI 53715
Phone: 608.263.6558, 608.263.3111
E-mail: randy.brown@fammed.wisc.edu

David H. Gustafson, PhD.
University of WI - Madison
Department: Industrial and Systems Engineering
1513 University Avenue, ME Bldg. Suite 4109
Madison, WI 53706
Phone 608.263.4882
Fax:608.265.3281 or 608.890.1438
Email: Dhgustaf@wisc.edu

Bruce Barrett, MD, PhD.
Department: Family Medicine and Community Health
1100 Delaplaine Ct Room 3832
Madison, WI 53715
Phone 608.263-2220
Email: bruce.barrett@fammed.wisc.edu

Ming-Yuan Chih, PhD.
University of Kentucky
Department: Human Health Sciences
900 South Limestone St Room 209
Lexington, Kentucky 40536
Phone: 859.257.2454

Email: m.chih@uky.edu

STUDY COORDINATOR: **Christine Stephenson, Ph.D.**

FUNDING SPONSOR: **National Institute of Health: National Institute on Alcohol Abuse and Alcoholism**

PARTICIPATING INSTITUTIONS:

The Center for Health Enhancement System Studies (CHESS)

The University of Wisconsin Department of Family Medicine and Community Health (DFMCH)

The University of Wisconsin School of Medicine and Public Health

The University of Kentucky

TABLE OF CONTENTS

STUDY SUMMARY

The purpose of this study is twofold: (1) to assess the impact a mobile health tool may have on reducing alcohol use and improving quality of life for patients with moderate to high risk drinking patterns and/or mild to moderate alcohol use disorder; and (2) describe how mobile health technology designed to support alcohol use reduction may be effectively integrated into primary care.

The primary aim of this study is to assess the impact on risky drinking patterns and quality of life for patients with risky drinking patterns or mild to moderate alcohol use disorder among patients who self-refer to our study from a primary healthcare system. Patients in the trial will be given versions of an evidence-based mobile-health (mHealth) system (A-CHESS) that is delivered using different implementation strategies according to study group. The original A-CHESS is an evidence-based, smartphone-delivered system characterized by the essential elements of relapse prevention: long duration,[1,2] assertive outreach,[3] monitoring,[4-6] prompts,[7-9] case management,[10-12] and peer[13-15] and family[16-18] support that was tested among patients exiting 90-day residential treatment for severe alcohol use disorder. A-CHESS has more than 18 services designed to improve social relatedness (e.g., online peer discussions), coping competence (e.g., guided relaxation and other interventions), and intrinsic motivation (e.g., reminders of why a patient wants and needs to control his or her drinking).

The version of A-CHESS to be tested in this trial maintains its core components but is modified to be appropriate for a self-referred study population in a primary healthcare system who are likely to represent a broad spectrum of patients who use alcohol. We have named this modified version of A-CHESS “Tula,” from the Sanskrit word for balance. We propose to randomly assign 546 patients who self-report moderate- to high-risk drinking patterns from UW Health clinics to one of 3 groups: 1). A self-monitoring group that receives information on alcohol, 2). A peer-supported group that uses the Tula system independently of the health system, or 3). A version of the Tula system that is clinically integrated in the health system.

Secondarily, we want to detect differences between groups in health system use, whether patients’ sex (male/female) moderates outcomes, whether effects are mediated by measures of competence, relatedness, and autonomous motivation, and whether levels of use of Tula correlate to changes observed in health outcomes (i.e., dose/response relationship). The study is designed to isolate and examine the role of the clinician in delivering an mHealth system. The cost-effectiveness of each approach will be assessed. This research examines a unique and promising mHealth system with potential clinical, economic, and societal importance and aims to determine the most cost-effective strategy for implementing mHealth into primary healthcare systems.

1.0 BACKGROUND & SIGNIFICANCE

Importance of improving outcomes for alcohol use disorders (AUD). According to the Pew Research Center's 2018 Internet Project Survey, 77% of adults in the U.S. owned a smartphone in 2018. The proliferation of smartphone use holds great potential for monitoring patients' chronic conditions outside the clinic setting. An increasing number of smartphone applications are designed to help patients manage their chronic conditions, such as diabetes and cardiovascular disease.[19,20] Studies in which clinicians monitor patient-reported data about chronic illnesses have shown better results with monitoring than without it.[21-29] Wisconsin ranks among the worst in the nation for heavy drinking and binge drinking among adults. According to the Wisconsin Department of Health Services, 22% of Wisconsin adults engage in binge drinking and 7% of Wisconsin adults engage in heavy drinking; nationwide[30], Wisconsin ranks 49th for binge drinking and 45th for chronic drinking.[31]

Barriers to effective treatment. Access and referral to necessary treatment represents an enormous barrier to treatment. Improving access to effective treatment is critical for a disease as pervasive as AUD and for which so few get treatment. In the U.S. in 2015, 26.9% of adults reported they engaged in binge drinking in the past month. By definition binge drinking is having 5 or more alcoholic drinks for males or 4 or more alcoholic drinks for females on the same occasion. About one in three adults 18 and older in the USA reported they drank excessively in the past month.[32] Given the prevalence of problematic drinking, it is evident that a large gap exists in the extent to which AUD is treated in primary care settings. Currently, the most popular and comprehensive primary care program for AUD treatment is SBIRT (Screen, Brief Intervention, Referral to Treatment). Patients who screen to have an AUD will receive a short talk about how to reduce their drinking, then will be referred to an addiction specialist. In a patient reported assessment, referral to treatment after screening only happens about 40% of the time.[33]

Advances in treatment and scientific knowledge. While mHealth is beginning to take hold in the clinical management of chronic conditions, the literature contains few examples in which patients and clinicians use patient generated data by mobile technology to manage AUD, even though AUD is a chronic, relapsing condition.[34-41] Patient self-management is fundamental to effectively treating AUD,[42] just as it is with other chronic diseases.[43] One mobile technology, A-CHESS, proved effective in a randomized clinical trial of recovering AUD patients.[44] We propose to use a modified platform of A-CHESS (as Tula) to find out whether mHealth can significantly improve AUD treatment in primary care settings. The proposed study also seeks to understand in what ways an mHealth system works and does not work, for whom, and under what circumstances. This new knowledge could have wide and lasting benefits in integrating mHealth systems for alcohol use disorders in primary care.

The Center for Health Enhancement Systems Studies (CHESS). CHESS focuses on two important areas of healthcare innovation: the use of technology by patients and family and implementation research. CHESS is home to the Network for the Improvement of Addiction Treatment (NIATx), the AHRQ-funded Center of Excellence in Active Aging Research, the

coordinating office for the Addiction Technology Transfer Centers, and research projects in family care, primary care, cancer, and dissemination and sustainability.

CHESS's current technology work focuses on smartphone applications. These apps are the latest evolutions in computer systems we have designed and tested for over 30 years with patients and family caregivers to improve health behaviors, quality of life, and access to care (chess.wisc.edu).[45, 46] The systems have been based on extensive needs assessments.[47-49]

Pilot tests (reported below) suggest that A-CHESS (Addiction – CHESS) will have positive effects on subjects who want to reduce their alcohol consumption:

1. In the first large randomized trial[50] studying the effects of mHealth on alcohol use disorders (AUDs), patients (n=349; 39% women) leaving residential treatment were randomly assigned to A-CHESS or usual care for 8 months and followed for 12 months. Over this period, those with A-CHESS had 57% fewer risky drinking days than those without it as well as longer abstinence. Participants used A-CHESS heavily, with nearly 60% still using it at 8 months.
2. In the most recent implementation research trial[51] which studied the effects of mHealth patients with a range of substance use disorders (n=268; 48% women) in federally qualified health centers (primary care clinics that serve patients regardless of their ability to pay) were provided access to an iteration of A-CHESS, called Seva, for 12 months. Over this period, patients had a 44% reduction in risky drinking days and improvements in self-reported quality of life. Patients sustained heavy use of the system over the 12 months across the three clinics. This suggests that Tula (the version of A-CHESS central to this study; see description, below) may prove to be an effective tool to reduce alcohol consumption in primary care patients.

Tula is a mobile health system based on A-CHESS but modified for self-referred patients in primary care who want to reduce their drinking. Participants are likely to represent a wide spectrum of patients, from those concerned about their drinking to those whose lives are seriously affected by their drinking. Patients randomized to all three groups in the study will download Tula on their smartphones and receive the same static content. This static content will appear in the following sections:

Thought of the Day—an inspirational quote intended to motivate participants.

Motivation—Participants can record, in words and photos, their reasons for wanting to work on their drinking and wellness; respond to a prompt to write a daily reflection; complete or revise What Matters to Me, about why they want to work on their drinking and wellness; and save favorites in Tula.

Tracker—Participants can set goals for 90 days—how many total drinks they'll have in a week and the number of days per week they'll drinking as well as goals related to other aspects of

wellness, such as exercise and sleep; keep track of their progress week by week; and take the weekly survey about factors related to drinking and wellness (mood, sleep, social pressure, etc.)

Information—Participants will see a library of information related to wellness, such as building healthy habits, reducing drinking, food and nutrition, physical activity, etc.

Relaxation—Information on relaxation techniques and audio recordings for meditation and binaural beats.

Strategies—Tips for reducing drinking and meeting other health goals, including "Rethinking Drinking" from National Institute for Alcohol and Alcohol Abuse, cognitive behavioral therapy, and quick tips for building skills related to making changes.

The content of Tula will vary by randomization group in two ways: the in-app communication services participants can access, and whether they work with a health coach, as follows:

- In the self-monitoring group, participants will not have access to a discussion group with others using the app. They will be able to send private messages only to the research coordinator (a member of the research team).
- In the peer-supported group, participants will have access to a discussion group available to all members of the group and moderated by a trained peer specialist. Participants will identify themselves in the discussion group by usernames they create, not by their real names. Participants in this group will be able to send private messages to others in the peer-supposed group as well as to the peer moderator. If participants have a question that the peer moderator cannot answer, he or she will refer the question to the research team.
- In the clinically integrated group, participants will have access to a discussion group available to all members of the group and moderated by a health coach. Participants will identify themselves in the discussion group by usernames they create, not by their real names. In addition, patients can send private messages to other members of the clinically integrated group and to the health coach. If participants have a question that the health coach cannot answer, he or she will refer the question to the research team. Participants in this group will be encouraged to have up to three sessions in person or by phone with the health coach at the beginning, middle, and end of the active 90-day implementation period.

We believe this RCT will have the following effects. (1) It will be the first RCT to test the impact on alcohol-related patient outcomes of mHealth in primary care. (2) Moderation and mediation analyses will help us understand how the elements have their effects on primary care patients. (3) We will better understand how sex relates to mHealth use and benefit. (4) We will test an mHealth system that offers essential elements of alcohol use reduction in a cost-effective and accessible way.

2.0 STUDY OBJECTIVES

This project proposes a hybrid type II effectiveness/implementation trial that will test the effect on risky drinking patterns and quality of life associated with patient use of an mHealth system under a variety of implementation

Primary Aim:

Detect the effectiveness of interventions by assessing the difference in self-reported risky drinking patterns and quality of life between subjects in the three study groups (self-monitoring, peer-supported, and clinically integrated groups).

Secondary Aims:

Because the study is designed to investigate both the effectiveness of Tula in primary care and the comparative effectiveness of different implementation strategies, the following secondary goals complement study's primary aims:

- Understand the significance clinician monitoring has on alcohol use interventions and patient outcomes.
- Calculate the costs of health system use for each group.
- Develop an mHealth reimbursement strategy prototype using CMS billing codes in the clinically integrated group.
- Understand the degree to which sex moderates the intervention outcomes among Tula users.
- Understand the degree to which patient competence, relatedness, and autonomous motivation (three tenets of self-determination theory) mediate the intervention effect in the Tula groups.
- Assess the dose/response relationship between Tula use and degrees of outcomes
- Understand the impact clinician monitoring has on AUD treatment.
- Qualitatively assesses clinician engagement and clinic needs to further refine Tula and its associated integration for future implementation and dissemination.

Sub-aim:

- Understand the relationship between pain and alcohol consumption after the 3-month active intervention.

Study Coordination

The Implementation Science and Engineering Lab is the coordinating site for this study. The UW study coordinator will oversee all activities at participating UW Health recruitment sites. Activities include:

- developing site-specific recruitment and data collection processes that meet study objectives;
- training the health coaches on protocol procedures prior to the start of recruitment and continuous monitoring to assure compliance with the protocol and human subjects regulation;
- communicating with site staff via regular conference calls to monitor progress, inform of protocol

changes/distribute new version of protocol, and address unanticipated issues or challenges;
- overseeing and managing recruitment of patients;
- following up with subjects who have completed the electronic recruitment and consent process;
- conducting voluntary qualitative interviews with clinic staff subjects (audio-recorded with permission); and managing all study data.

3.0 SELECTION OF SUBJECTS

Patients: A total of 546 men and women will be recruited from the UW Health academic medical center (e.g., primary care clinics, emergency medicine, and other entities of the University of Wisconsin-Madison for which the HS IRB is the IRB of record). Inclusion criteria:

1. Meet the criteria for at-risk drinking on the AUDIT screening (scoring 8+);
   OR respond yes to at least two questions on the AUD DSM-5;
   OR report moderate- to high-risk drinking patterns as defined by the NIAAA (i.e. more than 7 drinks per week and 3 on a single day for women; more than 14 drinks per week and 4 on a single day for men)
2. Are interested in learning about ways to reduce drinking and want to reduce or modulate their alcohol use
3. Are 21+ years old
4. Own an iPhone or android smartphone and are willing to download the Tula app
5. Are able to understand and sign an electronic consent form in English

Patients will undergo a 72-hour run-in period. Those who return to the app to submit a baseline and weekly survey during the run-in period will qualify to continue with the study and will be randomized to a study group.

Abuse or dependence on other substances will not exclude patients from participation. Patients whose eligibility screen results suggest the possibility of severe alcohol use disorder (at least 6 of 11 symptoms according to DSM-5 criteria) will be excluded. Patients who report having a current psychotic disorder that would prevent participation, have an acute medical problem requiring immediate hospitalization, or have a known terminal illness will likewise be excluded from the study.

When the study team notifies patients about their eligibility status, the team will encourage all ineligible patients to talk with their primary care provider to address any concerns they have about their alcohol use.

If the following scenarios occur during a patient's study period, the patient will remain enrolled in the study and their circumstances will be documented by the UW study coordinator: (1) is unreachable for follow-up surveys; or (2) becomes incarcerated. In the case of incarceration, no study data will be collected from incarcerated individuals during the time they are in prison or jail.

Site Staff: Up to 20 staff from participating UW Health clinics will be recruited to participate in interviews to provide feedback on the implementation of Tula. Interviews will take place with two distinct groups of staff:

1. Primary care clinicians are from a clinic that had at least 10 patients enroll in the clinically integrated group; and
2. Clinicians who participated in interviews during the development year.

4.0 REGISTRATION PROCEDURES

Patients

Recruitment. Study subjects who are patients at UW Health clinics will be recruited in many ways. The research team will implement one or two methods, assess effectiveness, and implement more if necessary:

1. *Recommendation.* Clinicians of UW Health Collaborative Care, such as primary care providers and behavioral health specialists, will recommend the study to potentially eligible patients who initiate a conversation about their alcohol use by giving them the flyer informing patients about the study and how to enroll. Potential subjects will be given the flyer at their appointments only once. As primary care providers and behavioral health specialists turn to telehealth to deliver care, providers may also provide information regarding the study via the additional channels described below. In each situation, recruitment materials supplied to clinicians will be shared with potential participants at the discretion of the clinic and/or clinician and are informational in scope: subjects will ultimately self-refer to the study.

2. Emergency Department Research Coordinator: An Emergency Department Research Coordinator, who is a staff person employed by the Department of Emergency Medicine, will monitor the HealthLink trackboard for eligible patients. The trackboard will notify them of individuals who may be eligible. Patients they visit will have a positive AUDIT-C screen (score of 4+ for men; 3+ for women). EDRC study staff with UW Health electronic health record (Health Link) access may also use tools made available to them as part of their research access to Health Link, including searching patient list templates or receiving automated alerts (use of a silent BPA-best practices alert), to help identify potential subjects for study enrollment evaluation. This pre-screening eligibility review of medical records will be used to identify the subjects to be approached. These staff members have a broader role in the ED. They complete duties as assigned by the Department Chair as it relates to the overall mission of the Department of Emergency Medicine (e.g., research, clinical operations such as quality improvement, communication, & process monitoring, etc.). These RAs, under the direction of the ED clinical providers, will approach subjects and inform them about the study by offering the flyer and answering any questions.

3. *Flyers*. Recruitment flyers will be placed in UW Health clinics and other relevant facilities (UW Hospital, community centers, etc.) with permission from the hosting organization. Flyers will specify the inclusion criteria and requirements for patients to self-refer into the study; provide contact information for study staff, a means for interested individuals to request more information or ask questions; and direct potential participants to the online screening survey.

   As a recruitment strategy, thoughtful placement of recruitment flyers aims to promote the study by increasing its visibility. Effective March 2020, the necessary and widespread constraints, restrictions, and closures occasioned by the COVID-19 pandemic response significantly undermines this strategy. As an extension of flyer placement in strategic locations, the study team will pursue alternate spaces, both traditional and internet-mediated, for hosting the information represented in the flyer. In some cases, the information will be adapted only insofar it is necessary to fit the space and will preserve the content and language, if not necessarily the design, of the existing IRB-approved flyer. These alternatives include:

   a. *Health newsletters and digital communications.* As a component of our recruitment strategy, we will seek opportunities to promote the study through health newsletters, including e-newsletters. Such newsletters typically operate as a service to patients as an extension of a health system, health care organization, or other relevant professional body and provide wellness tips and resources from health experts to help its constituents maintain a healthy lifestyle. We will adapt the information from the IRB-approved study flyer for these media, including contact details for the study team should interested individuals wish to learn more or ask questions about the study.

   b. *Websites.* With permission from the hosting organization, and in compliance with each site's terms of use, we will seek to promote the study on websites appropriate for an eligible participant population, including but not limited to the Department of Family Medicine and Community Health, the Implementation Science and Engineering lab (home website for the study), and other relevant professional bodies and interest groups. Information provided to each hosting website will rely on the language and information included in the existing IRB-approved flyer and/or use a digital file format of the same.

   c. *Traditional media outlets: television, radio, and newspapers.* In consultation with UW Communications' News & Media Relations, we will explore and, where appropriate, pursue opportunities to promote the study through traditional media channels using the information contained in the existing flyer. We will limit our activity in these traditional media channels to communication tactics that serve only to offer public notice. These may include purchasing advertising space or issuing an informative press release,

   d. *Social media.* The study team proposes limited use of social media to increase the visibility of the study under these strict conditions and in compliance with HIPAA standards: 1) information from the flyer will be posted only under conditions that neither allow nor support public comment; 2) eligibility criteria, as presented in the flyer, is clear and explicit; 3) the study team will only interact with potential participants to address questions about the study through the

means (phone or email) presented in the flyer.

4. *Community outreach*. Historic distrust of medical research has resulted in lower participation rates from underrepresented populations. Recruiting from communities of color requires building relationships within those communities via direct personal contacts. With their permission, flyers will be sent to community centers and other community organizations that serve in those neighborhoods where information can be provided to their residents. Directors of those community organizations will be instructed to refer any interested participants to the study team for more details.

Screening and Enrolling in the Study. No subjects will be coerced to enroll in the study. Interested subjects will be directed to a website (isel.wisc.edu/screen) to complete an initial screening survey via Qualtrics. Potentially eligible participants will consent that they are submitting data for a screening which will assess eligibility. During the eligibility screening, patients will be asked to provide their e-mail address (to be notified of their eligibility and to receive the $10 Amazon.com Gift Card (digital code) and their zip code to verify their residency within the UW Health service area). Individuals will be informed that email is not guaranteed as a secure means of communication. Scripts for communicating screening participants' eligibility status have been uploaded to ARROW.

All screening survey results will be reviewed by study staff, who will notify all who complete the screening survey of their eligibility or ineligibility. The screening survey is not intended to diagnose AUD, but if an individual is found to be ineligible based on DSM-5 scores that are consistent with severe AUD, the individual will be notified that they are not eligible. These individuals, as well as all others who screen ineligible, will be encouraged to talk about their drinking with their primary care provider, who is qualified to provide resources and/or refer them for evaluation and treatment (see Post-Screen Script – Not Eligible in ARROW). Data (except age, biological sex, and reason for exclusion) from ineligible participants will be destroyed.

Individuals who screen eligible for the study will be notified via email and invited to enroll in the study. Instructions for downloading the app and enrolling in the study are optimized for digital methods of communication and include links to download the app, available in the Apple App Store and on Google Play (see attached "Post-Screen Script -- Eligible" in ARROW). Participants will be asked to download the Tula app within 48 hours of receiving the invitation to join the study. If a participant has not downloaded the app after 48 hours, the study team will send up to 2 reminders over a 2 week period, provided the participant granted the study team permission to send them reminder emails at the time of screening. Screening data from eligible participants will be recorded in Qualtrics. Once screening data has been reviewed, the data will be removed of identifiers, coded, and stored on a secure server at HIP.

Consent. The following two-step consent process will occur within the Tula app on the patient subject's smartphone. After the individual has downloaded the app, they will be presented with Informed Consent #1, which requests their broad consent for the study. This consent includes detailed information applicable to all participants in the study, regardless of randomized group

assignment, and a step-by-step process overview of their activities—including their immediate next steps for completing their enrollment (comprised of the 72-hour run-in and Consent #2). Upon completing Consent #1, participants will be asked to create a Tula account. Once created, they will be asked to complete the items on the Quick Start Checklist. Patients who do not complete the checklist tasks will not be randomized and all collected data (except age, biological sex, and reason for ineligibility) will be destroyed. Age, biological sex, and reason for ineligibility will be kept for generalizability and reporting reasons. Randomization (see below) occurs after patients complete the checklist tasks during the 72-hour run-in period.

The research team will use the private messaging feature in Tula to schedule a phone call with individuals who remain in the study. During that call, a member of the research team will confirm the participant's consent, answer any additional questions about the study that the patient has, and will randomize the individual to one of three groups of Tula users. Once randomized, patients will be prompted to complete Informed Consent #2 via the app, the next time they login. Informed consent #2 serves as an addendum to Consent #1 and provides detailed information specific to the patient's assigned group.

Patients are advised to take their time reading the consent forms; they may leave and return to them and reread sections if they'd like to. To mitigate any potential difficulties related to readability (i.e. length of the document, screen size, small text) and to ensure participants understand the most critical aspects of their participation in the study, we will preface the full text of the consent form with a bulleted list, highlighting in plain language the following sections: what the study is about, how we will protect their confidentiality, benefits and risks involved, remuneration, voluntary nature of participation, their participation and their healthcare, and contact information for questions. Subjects will also be able to listen to a verbatim recording of each consent form using a screen reader. If the subject has not agreed to the informed consent after two weeks, he or she will no longer be able to join the study and all data collected during the screening process will be destroyed (except age, biological sex, and reason for exclusion, per CONSORT standards), A copy of the consent form will be accessible to the study coordinator via the Tula server. Subjects can refer to the consent forms electronically by navigating to the Study Information sections of Tula. They will also be able to email the consent form to themselves. If a subject declines to participate at any time during the consent process, he or she may select a "I choose to not participate" button that will ask them why and return them to the launch screen. Reasons for refusal will be noted, in line with CONSORT standards.[57] Subjects who choose not to disclose why they are ending their participation in the study will also be able to say "I choose not to respond" or "none." All subjects will be reminded that they are under no obligation to participate in this study and can withdraw from the study at any time. They are also told that their health care will not be affected by their participation in this study. Once subjects opt out of the study, they will no longer have access to Tula.

Randomization. Randomization will be done by the study coordinator using the urn randomization program and happen prior to informed consent #2. Study staff will access the admin tool within Tula to assign patients to the self-monitoring, peer-supported, or clinically integrated groups. Randomization will be done in block randomization by clinic, sex, and severity of alcohol use.

Following randomization, study staff will call the individual to notify them which group they are in and explain what is required of them.

Patients will need to install just one version of Tula because the features patients have access to will be modified according to the randomization group.

Patients in all groups will be asked during the consent process to allow monitoring of their Tula usage by the research team to determine which parts of Tula are most helpful; patients randomized to the clinically integrated group will have the option to share information from Tula with the health coach at UW Health. All data shared from patients to the UW Health health-coach will be initiated by the patient.

Remuneration. Participants who complete the screening survey will receive a $10 digital Amazon.com Gift Card in the email sent to communicate their eligibility status, regardless of their eligibility. .

In all recruitment scenarios, subjects will be told the study incentives ($10 for completing the eligibility screen; up to $250 for enrollment and participation in the study) and how to earn them in the study:

- complete baseline measures in the Tula app, for which subjects will be paid $30;
- complete weekly surveys for the first 12 weeks of the study, for which subjects will be paid $10 per completed week (all groups);
- complete 4 quarterly surveys (between months 3-12), for which participants will be paid $20 each;
- earn a bonus of $20 for completing all surveys

Incentives will be distributed monthly to subjects by digital gift code. If subjects prefer to receive incentives via e-mail, they must grant the study team permission to use their email address for this purpose; otherwise, monthly incentives will be delivered securely through the in-app communication tool (private message). Subjects will be notified of this information when they formally consent to participate in the study .

For the participant interviews, each participant will receive a $50 gift card in remuneration for their time.

Clinic Staff

Recruitment and Consent. Site staff (up to 20) eligible for interviews will be 1) primary care clinicians who the study team interviewed in the development year and 2) providers from clinics that had at least 10 patients in clinically integrated group. Primary care clinicians, whom the study team interviewed in the development year (IRB ID 2018-0885), will be recruited by emailing them to ask if they would like to participate in an interview after the intervention period is complete (intervention

month 36). Interviews will be used to assess the implementation process (what worked well, what did not work well, and whether and how clinicians valued Tula).

At baseline, participants will be asked what their home clinic is. Clinicians of clinics that had at least 10 or more patients in the clinically integrated group will be contacted by email. The email will ask the clinicians at the end of the study if they want to participate in an interview to share information about his or her experience and feedback related to Tula. Details of the study and their participation will be explained and if they agree to participate in the study, signed informed consent will be collected in person.

Participant interviews

We will recruit 9-18 participants total across the three study arms (self-monitoring, peer-supported, and clinically integrated). Participants will be currently active participants as well as participants who already completed their 12 months of the study. Based on data assessed by use engagement data and engagement in discussion group forums, we will recruit participants who are/were heavy users of the Tula app and those who are/were light users of the app. For participants in the peer-supported and clinically integrated groups, we will also recruit participants who are/were or were not engaged with either the peer support specialists or health coaches. Lastly, we will recruit participants who were active in the discussion group forums. A waiver of signed consent will be sent to participants to review. We will review and ask for verbal consent prior to the interview. Interview questions will use the domains of the CFIR framework to explore participants' experiences with the app and, for those randomized to these study groups, the health coaching and the peer mentoring. Sample interview questions for each domain are shown below. Members of the research team who have received training in qualitative interviewing will conduct the interviews. Interviews will be conducted via a secure video conference call (Zoom) and will be audio recorded. Each participant will receive a $50 gift card in remuneration for their time.

CFIR Domain	Sample Interview Questions
Inner context	Overall, did Tula help you to reduce your drinking? • If yes, probe for how it helped • If no, probe for why it didn't help and how it might be changed to be more helpful Are there people for whom Tula is going to be a better fit than others? • Probe for explanation of answer.

Outer context	We know that the pandemic was a hard time for a lot of people. How did you do during the pandemic? • Probe for how pandemic affected their drinking • Probe for whether pandemic affected the ways they used Tula
Innovation	I'm so glad to have the opportunity to talk to you so I can understand more about your experience using Tula. To begin, please tell me why you decided to join the Tula study? How did you use the app? • Probe for components used [have list of components and prompt if the participant does not mention using them] For PM group, tell me about your experience with [the PM]. What suggestions would you have for them to improve the experiences of people using Tula? For the HC group, tell me about your experience with [the HC]. What suggestions would you have for them? What was most valuable to you about using Tula? What was most frustrating? How could Tula be improved? If you had a friend who wanted to reduce their drinking, would you recommend Tula? • Probe why or why not • If yes, probe what they would tell friend about how to get the most out of the app.
Bridging	What technical support did you need to help you use Tula?

	Did you get that support? What suggestions do you have for how that support could be improved?

5.0 INTERVENTION PLAN

All patients enrolled in the study will participate in a 3-month intervention period followed by a 9-month follow-up period, for a total of 12 months. Patients are allowed to continue using Tula after the 12-month period, but will not be asked survey questions after 12 months. Please note that Tula is not a treatment—it is a resource used to help patients reduce their drinking.

All patient subjects will undergo a 72-hour run-in period when they will have access to the basic version of Tula. During this period, potential subjects will be asked to complete the Quick Start checklist items within the 72 hours. The checklist tasks are completing the baseline survey; setting goals for the 90-day active intervention period related to drinking and, optionally, to other aspects of health (e.g., sleep, exercise); completing the first weekly survey; and completing a survey called What Matters to Me, which helps patients think about their current health status and what they would like to change. After 72 hours, patient subjects who complete these tasks will be randomized to one of three groups and receive the appropriate access to Tula features.

Patients in all three groups—regardless of randomization group—will have access to the same static content on Tula, which is described in Section 1, Background and Significance. In addition, patients in all three groups will be asked to complete (1) a weekly survey during the active intervention period and, optionally, to revise the goals they set during the run-in period and (2) quarterly surveys at month 3, 6, 9, and 12. Subjects are free not to answer any survey questions.

Self-monitoring (control) group. Patients of this group will continue receiving regular care from their physician with no interference from the two experimental groups. No data will be shared with other participants. Only the research team will have access to subject data for evaluation purposes.

Peer-supported group. In addition to the static content available to patient subjects in all three groups, patient subjects in this group will have access to a discussion group where they can message one another and have the ability to share and see posts of other patients. The only involvement of someone other than patients themselves in the peer-supported Tula group will be by a trained peer mentor (i.e., a dedicated Tula user from the area with a sustained history of successful alcohol reduction). The peer mentor will participate in Tula discussion groups, moderate the discussions, and encourage use of the system (e.g., by posting topics in the discussion group, pointing Tula users to a potentially helpful tip). The peer mentor will not have access to individual Tula use data. Patient-reported feedback will be presented directly to the patient only. The peer mentor will be introduced to

the study by the study coordinator and receive access to Tula for 36 months.

Two Certified Peer Specialists from Safe Communities of Madison-Dane County will provide participant mentoring and discussion forum moderation for the peer-supported group. These peer specialists, who will serve as peer mentors for the study intervention, completed the CITI Human Subjects Research Training: UW Biomedical Course using the materials and attestation form provided by UW's Human Research Protection Program (HRPP) and have been added to the IRB study record as external personnel.

Clinically integrated group. In addition to receiving the same static content available to all patients, patients in the clinically integrated group will also have access to a discussion group with others in the group (like the peer-supported group described above) and access to a health coach from the UW Health Wellness Center. Health Coaching at UW Health's Center for Wellness at the American Center is provided by a Certified Wellcoach, either in-person at the American Center or over the phone. Health Coaching sessions are not scheduled via Health Link: Health Coaches directly and independently manage their own client calendars. Patients schedule a session directly with the Health Coach via phone or email. When the Health Coach sees a client for more than one session, they schedule the first session via phone or email, then set up subsequent sessions during the first session. Standard clinical Health Coach appointments are not documented in any way in in Health Link, nor will they be for this study; as an out-of-pocket, open-to-the-public service, The Center for Wellness uses an independent third-party system, ActiveNet, for any billing needs.

Patients will be encouraged to participate in up to three in-person or phone visits with the health coach at the beginning, middle, and end of the active 90-day implementation period, with the first visit lasting between 60 and 90 minutes and the other two lasting between 20 and 45 minutes. The health coach will also function as the moderator of the discussion group, as the peer mentor does in the peer-supported group.

Patients will have the option to share selected Tula data with the health coach through a dashboard. When a patient in this group completes a survey, they will be presented with a question: "Do you want to share your responses with the health coach? Yes/No." If the subject responds "yes," their survey responses will populate a dashboard that contains data on drinking days / drinks per day and other data reported via the weekly survey. The health coach will have the option to view the data in the dashboard. Data in the dashboard will not be placed in the patient subject's electronic medical record. However, if the health coach sees any data that is concerning that would normally prompt follow-up within the scope of their clinical role, the health coach will contact and follow-up with the patient subject if such a situation were to arise.

The UW Health Coach at the American Center is not professionally obligated to communicate with a patient's PCP; in most coaching circumstances, the Health Coach would not know the identity of a patient's PCP, and having an established relationship with a PCP is not a prerequisite for inclusion in

the study or health coaching in general. That said, there may be circumstances where action/communication may be warranted if a subject discloses information that has a direct bearing on his or her health. The Wellness Center has several primary care providers on site at the American Center that the health coaches involved in this study routinely consult in such circumstances.

This sensitive health information being collected and shared through the Tula dashboard allows the coaches to be better informed and provide more responsive treatment. Information shared via the dashboard serves only to support the intervention and will not be used as study data; no response is expected of the health coach relative to her research role. Health coach communication with a patient in the course of the intervention will be dependent on the individual health coaching plan the patient creates with the support of the health coach in accordance with the Whole Health model used by the health coach. If a patient declines to share data to the dashboard, no data will be transmitted to the dashboard.

To schedule the first of three coaching visits, which may take place on-site at the UW Health Center for Wellness or via phone conversation, the health coach will use the private messaging feature in Tula. Subsequent visits may be scheduled during that first 60-90 minute visit or via the app's private messaging feature, depending on the patient's preference. During the consult, the health coach will review "What Matters to Me," the Wellness Center survey patients complete during the run-in period. The health coach will work with the patient to form a vision of what their health could be by asking the patient "What do you want your health *for*?", helping the patient develop a short-term goal, and formulate an action plan. Following the initial coaching session, the patient may use Tula to journal about their experiences so they can refer to this information during brief weekly or bi-weekly follow-up encounters with the health coach, which will take place via private message over Tula, and/or during their two subsequent health coaching visits. The health coach will ask patients how they are doing, how they are progressing toward their goals, where they want to go from here, and how they want to get there. The health coach will provide structure for the patient to achieve their self-identified goals.

Clinic staff. Clinic staff will be asked to participate in interviews in a private room at their clinic. The study team will interview two groups of clinicians: 1) the primary care clinicians who the team interviewed in the developmental year and 2) clinicians at clinics that have had at least 10 patients (in the clinically integrated group) using Tula. Interviews will take place once the intervention phase of the study is complete. Clinic staff subjects will be informed of the study and sign an informed consent. Subjects will be reminded that their participation is voluntary, that they do not need to answer any questions they do not want to answer, and that they may leave the interview at any time. The study team will ask open-ended questions about the implementation process of Tula such as what barriers to implementation the clinic experienced, what worked well, and what can be improved upon for next time. Clinicians will also be asked the "Iowa A-CHESS value for clinic managers" survey. The interview will be recorded and transcribed by a member of the study team. During transcription all names will be coded and any identifying information will be removed.

External Research Site and Personnel

Safe Communities of Madison–Dane County is a local non-profit [501(c)(3)] coalition that brings together public and private sector partners to save lives, prevent injuries, and make the community a safer place. The organization focuses on projects and programs with a track record of positive impact and success and has been involved with research projects and initiatives at UW–Madison and UW Health since its inception in 1999. As a community partner for this study, Certified Peer Specialists employed by Safe Communities will provide in-app peer mentoring and discussion forum monitoring/moderation for the study arm receiving the peer-supported intervention. Certified Peer Specialists recognized in the State of Wisconsin complete peer support training, examination, and continuing education requirements specific to both mental health and substance use-oriented lived experiences. Safe Communities of Madison–Dane County is accredited under guidelines established by the World Health Organization Collaborating Center on Community Safety Promotion, National Safety Council's Safe Communities America Network and Pan Pacific Network of Safe Communities.

Data collection.

Table 1 shows the data collection for the study, including source, burden, and timing.

Table 1: Quantitative Outcomes

Dimension	Measure	Source	Burden	Timing (after rand.)
Patient Outcomes				
Risky drinking patterns	Timeline followback[58,59]	Patient survey	5	0, 3, 6, 9, 12 mo.
Quality of life	PROMIS Global Health[60]	Patient survey	10	0, 3, 6, 9 ,12 mo.
Willingness to share data	Number of participants opting to share Tula data with clinicians	Tula	NA	Continuous
Cost				
Healthcare utilization	Medical services utilization form[61]	Patient survey	4	0, 6, 12 mo.
Implementation costs	Clinician experience with implementation of Tula.	Staff interview	60 min.	Once, after the intervention is complete.
Other Outcomes				
Risk/protection factors	Brief Alcohol Monitor [63]	Patient survey	10	0, 3, 6, 9, 12 mo.
Specialist report use (clinicians)	Number of days used	Server log files	NA	Continuous
Alcohol use severity	AUDIT	Patient survey	10	Pretest, 12 months
AUD severity	DSM-5[64]	Patient survey	11	
Patient and clinician decision making	Value and decision framing survey	Patient/ clinician survey	9	Patient: Pretest, 12 months Clinician: during interview at month 36
Mediators				
Relatedness	CHESS Bonding Scale[48,65]	Patient survey	5	0, 3, 6, 9, 12 mo.
Competence	Perceived Competence Scale	Patient survey	4	
Autonomous motivation	TSRQ[66]	Patient survey	6	
Tula use (patients)	Number of days used, number of pages viewed	Server log files	NA	Continuous
Moderators				
Patient characteristics	Race, ethnicity, gender, age	Patient survey	NA	Pretest

All survey data collected through Tula is housed on CHESS servers then exported to the UW sponsored Google Drive folder for statistical analyses.

Screening survey: People interested in participating in the study will be directed to take a Qualtrics screening survey hosted on the Web to determine if they are eligible to participate in the study.

Baseline survey. After patient subjects are enrolled in the study, they will be asked to take a baseline survey consisting of demographic questions, medical service utilization, quality of life, a modified version of the Brief Alcohol Monitor, the CHESS bonding scale, the alcohol competence scale, the TSRQ, and the value of Tula. Data from the screening survey will be used as baseline data for the AUDIT, AUD DSM-5, and timeline follow-back. Two additional questions related to the impact of COVID-19 on participants' physical and mental health will be added to the quality of life measures. These questions will operate on a 5-point Likert scale and will be included across all CHESS studies. (See supporting document "4.6.20 Global Health Scale v1.3_COVID.docx").

Quarterly follow-up surveys. Starting at month 3, patient subjects will be asked to take surveys once every 3 months. The study team will ask patient subjects to take the following surveys: 1) quality of life, 2) a modified version of the brief alcohol monitor, 3) timeline follow-back, 4) CHESS bonding scale, 5) alcohol competence scale, 6) TSRQ, 7) medical services utilization (6 months and 12 months only), 8) AUD severity (12 months only), 9) value of Tula (12 months only), 10) quality of life and 11) AUDIT. Two additional questions related to the impact of COVID-19 on participants' physical and mental health will be added to the quality of life measures. These questions will operate on a 5-point Likert scale and will be included across all CHESS studies. (See supporting document "4.6.20 Global Health Scale v1.3_COVID.docx").

Use data. The app automatically collects use data by placing "cookies" on subjects' smartphones (with patients' consent) when randomization takes place. Data are stored on a secure central server at CHESS.

Qualitative interviews. In order to better understanding the implementation of Tula in the health coaching and peer mentoring organizations, the study team will use the CFIR framework to interview the two health coaches and four peer mentors, as well decision makers in these organizations. In order to better understand the conditions under which Tula can be sustained, the team will conduct interviews with organizational decision makers and health system decision makers. Sample questions for each of these interviews are shown below. Interviews will take place at month 36 and last 30-60 minutes. Members of the research team who have received training in qualitative interviewing will conduct the interviews. Interviews will be conducted via a secure video conference call (Zoom) and will be audio recorded. Participant identities will be protected. Any identifiers will be coded in the transcripts so that there will be no way to link clinicians to their interview responses. Data collected will be used to refine the system for future dissemination.

For health coaches and peer recovery workers **CFIR Domain**	**Sample Implementation Questions**
Inner Context	How would you describe your role in Tula? Please walk me through everything you did related to Tula. Probe for both interpersonal (inc. discussion facilitation) and logistical work. Probe for what worked well and what didn't relative to the interpersonal and logistical tasks. Probe for what was gained ad what was lost by doing everything virtually. In what ways did your work on Tula fit well with your broader role here at [organization]? In what ways was it a poor fit? Is Tula's harm reduction philosophy consistent with the philosophy at [organization]? If yes, tell me more about how it is consistent? If no, tell me more about how that affected your work with Tula? Thinking about [your organization], what do you have in place here that made it possible for you to do your Tula work? What were the barriers?
Outer Context	Other than [things mentioned within organization that

	supported Tula], what helped Tula to be successful? And what got in the way of that success? How did the pandemic shape your experience? How did the pandemic affect the experience of people using Tula? Which users seem to benefit from Tula? What tells you this? What about users for whom it didn't seem to work?
Innovation	I'm interested in learning about how you think about how people change. Specifically, please tell me what you understand about how people reduce their alcohol consumption? In what ways does Tula help people in reducing their alcohol consumption? In what ways does it fall short? How should Tula be changed to work better for folks in making this change?
Bridging	Thinking about the Tula team [name individuals], what did they do that was most important to supporting you in working with Tula? What could be improved?

For HC/PM decision-makers **CFIR Domain**	**Sample Implementation Questions**	**Sample Sustainment Questions**
Inner Context	What is your role at [organization]? What role did you play in implementing Tula at [organization]? Thinking about [your organization], what do you have in place here that made it possible for you to implement Tula? What were the barriers to implementation? Is Tula's harm reduction philosophy consistent with the philosophy at [organization]? If yes, tell me more about how it is consistent? If no, tell me more about how that affected [organization's] implementation of Tula?	Who at [organization] would make the decision about making Tula part of your regular service offerings? What would matter when making this decision? What steps would need to taken in order to make Tula part of your regular service offerings? What would need to be in place at [organization] in order for you to make Tula part of your regular service offerings?
Outer Context	Other than [things mentioned within organization that supported Tula], what helped [organization] to implement Tula? And what made implementation difficult?	What would need to be in place external to [organization] in order for Tula to be made part of your regular service offerings?
Innovation	What's your overall assessment of Tula? What's the value of Tula? • For users • For the work that you do here at [organization]	How could Tula be improved to enhance [the value of Tula they have described]?

Bridging	Thinking about the Tula team [name individuals], what did they do that was most important to supporting you in working with Tula? What could be improved?	What can the Tula team do now that would make it more likely that [organization] would make Tula part of its regular service offerings?

For health system decision makers **CFIR Domain**	**Sample Sustainment Questions**
Inner Context	Who at [organization] would make the decision about making Tula part of your regular service offerings? What would matter when making this decision? What steps would need to taken in order to make Tula part of your regular service offerings? What would need to be in place at [organization] in order for you to make Tula part of your regular service offerings?
Outer Context	What would need to be in place external to [organization] in order for Tula to be made part of your regular service offerings?
Innovation	Knowing what you know about Tula, which needs at [organization] might it fill? What changes could be made to Tula that would improve its ability to meet those needs?
Bridging	What can the Tula team do now that would make it more likely that [organization] would make Tula part of its regular service offerings?

Remuneration. No remuneration will be provided to these participant groups.

Unanticipated Events
Should any unanticipated problems arise, the research team will work with the HS IRB to address the problems according to posted IRB guidance. The following is intended to further clarify some possible scenarios.

If a patient (1) stops receiving treatment at one of the participating clinics or (2) becomes incarcerated, the patient will remain enrolled in the study and their circumstances will be documented by the UW study coordinator.

In the first case, the patient would continue to complete surveys and use Tula if applicable per the study protocol.

In the second case, no research activities would occur during the time of incarceration. If the patient is released during the study period, s/he can contact the study coordinator to continue in the study, if s/he would like. The reason for any missed data will be documented.

Subjects may sometimes use Tula inappropriately. Discussion group moderators will review and delete any discussion board messages deemed inappropriate (i.e., those containing nudity, threats, racism, and bigotry). A research staff member will then follow up with the author of the inappropriate content.

Cases in which a subject has ongoing borderline behavior will be evaluated individually and the subject may be removed from study if the research team feels it is in the best interest of the subject as well as the others in the study.

Privacy and Confidentiality
To mitigate the risk of patient breaches of confidentiality, all patient subjects will choose a username when they create an account. A list of patient subject usernames will be kept by the research team PI and stored in a secure, limited access, password-protected file service on HIP servers, which are located in the University Bay Office Building. Any hard copy identifying information will be stored in a locked cabinet. Other identifiable data entered into Tula by the patient subject will be removed by Adam Maus, the CHESS data security officer, before it can be accessed by the research team. Adam Maus acts as an honest broker at CHESS for the patient data collected through Tula; the study team will also request that Tom Callaci, SMPH honest broker, confirm that the dataset s de-identified before it is uploaded to Google Drive. During account creation, the Tula system will assist patients in choosing a username and password to log in to the Tula system. Patients will be instructed not to use their real names or other identifying information as a username and will be made aware of the potential dangers of divulging confidential information (e.g. real names or telephone numbers).

Subjects in the clinically integrated group who decide to share their Tula data with health providers may choose to stop sharing at any time. Subjects will be asked whether or not they want to share data with the health coach each time they enter data in Tula, and have the option to stop sharing their data permanently and retrospectively by going to the app privacy settings and selecting the option “do not allow others to see my data.” In this case, the health coach would not see anything about the patient’s participation and only the research team would have access to the subject’s data.

No data collected by Tula will be entered into patients' electronic medical record or affect the legal medical record.

Clinician interview data will be recorded using secure encrypted, password-protected recording devices. The recording will be transferred to the Health Innovation Program password-protected servers as soon as possible and deleted from the recording device. Recordings will be transcribed, coded, and removed of all identifying information. Once the recording is transcribed, the recording will be deleted from the server.

Participant interviews will audio recorded and transcribed by a HIPAA approved service from the Wisconsin Surgical Outcomes Research program. All data will be coded, de-identified, and assigned a study ID. Any identifying information will be stored separately in a password-protected server as soon as possible. Once the recording is transcribed and the transcript is spot checked for accuracy, the recording will be deleted from the server.

Potential Risks
The main risks are the potential for subjects to receive and act on bad information or misinterpret accurate information, and the potential that confidentiality of the subjects' records will be breached. More specifically:

- Depending on the method of recruitment and how a participant learns about the study, it is possible some participants may feel compelled or obliged to participate because the recommendation comes from a person deemed by the participant to be in an authority position. Participants may be concerned about maintaining their standard of care. Every effort will be made to clarify to participants that their care will not be affected whether they participate or not.
- Through screening processes, which derives its questions from AUDIT and DSM-5 questionnaires, individuals' responses may suggest symptoms of an undiagnosed severe case of alcohol use disorder. This may be upsetting to them, especially in the context of not being able to take advantage of the resources/support provided in Tula. Like all participants who screen ineligible, these individuals will receive either an email or a phone call, per the communication preference they selected during the screening survey, informing them that they are not eligible for this study. They will be encouraged to talk with their primary care provider about their alcohol use. Patients do not have to follow through on the recommendation to receive treatment.
- Patient subjects in the clinically integrated group could be disclosing possibly stigmatizing alcohol use data to the health coach that may affect treatment at UW Health. We will mitigate this risk by giving the patient subject the option of choosing which data, if any, to share with the health coach. Consent forms will make it clear that any data that the patient does not want to share will be not be available to the health coach and by extension any providers within the UW Health system. Furthermore, Tula data will not be entered into the patient's electronic medical record.

- Tula could provide inaccurate or harmful information. The information will carefully vetted by experts from the clinics (Dr. Brown), the study team, and UW CHESS's Steering Committee. Network communications between subjects will be monitored. Inaccurate or harmful statements will be addressed by the Tula moderator. Additionally, messages exchanged within the Tula support groups will be monitored to make sure the information is accurate and that study participants are using the system for its intended purpose.
- There could be a breach of confidentiality that could result in disclosure of research data outside of the study team. This could carry economic or legal risks for subjects. To prevent this, all subjects will be assigned a de-identified code number (separate from the username). These lists will be kept in a locked spreadsheet on the HIP servers, and will not be shown to anyone except study staff. Data collected from smartphone use files will have the name removed and the code number attached by the research team study coordinator. Interviews will be conducted by research staff trained in human subjects training.
- There is risk that information provided in Tula will be used to the detriment of the subjects. Particular sources of risk include email and newsgroups, as well as Tula communications written within the discussion groups or personal profiles. Patients will create an account with a username and password to use on Tula. They will be instructed to not use their real name as a username and will be warned of the potential dangers of divulging confidential information (e.g. real names or telephone numbers). Patients will also be asked in the informed consent and given directions to set up a passcode on the phone to protect their information in the event someone else finds the phone.
- There may be a stigma attached to using Tula. There are times and contexts when notifications of weekly or monthly surveys draws unwanted attention. In these instances, study participants can set their smartphones to vibrate so they are subtly prompted to complete their weekly check-in survey , and they can also have the option to prompt the system to remind them later for a check-in at a more appropriate time.
- Participants may send messages when moderators cannot respond quickly. Offering features could produce over reliance on Tula to provide support during periods of distress. Study participants will be told that the moderator of their discussion group will make every effort to follow-up on their messages for support. If the moderator is not immediately available, the app will let the participant know that a moderator is unavailable and if they need immediate assistance they should contact their UW health clinic. To maintain a separation between research and clinical activities, members of the study team will not forward patient messages to the central desk of their UW health clinic.

Additional risks may include:

- Learning about sensitive issues, such as excessive alcohol use, while using the Tula app may cause anxiety, distress, embarrassment, or feelings of sadness. However, patient subjects do not have to answer any questions that they don't want to answer.
- The research team will be collecting information on how the smartphone is used and may discover behavior that raises concern about harm to self or others. If we see anything that

suggests that patient subjects or others face imminent risk of harm, we will contact appropriate others to intervene (e.g. the police). Individuals will be told this during informed consent.

- All clinicians who are interviewed will be told that they do not have to answer any questions they do not wish to answer. The study team will have any identifying information coded and removed from transcripts. The code key will be kept separate from the transcripts in a locked cabinet. After transcripts are made from recordings of the interviews, the recordings will be destroyed.

To further protect subject confidentiality, all studies funded by the National Institute of Health are issued a Certificate of Confidentiality which prevents investigators and institutions from being required to release identifiable subject information.

Data Storage and Protection

CHESS and HIP servers are separate servers. All data collected through the Tula app will be stored on CHESS password-protected servers. CHESS programmers will create de-identified data exports and uploaded to a UW-sponsored Secure Box where it can be accessed for statistical analyses by UW study members and Ming-Yuan Chih of the University of Kentucky. All data collected outside of Tula (interview transcripts, code keys, etc.) will be stored on HIP password-protected servers.

When all study activities are complete, audio recordings, participant IDs, and other identifiable information will be destroyed; only the de-identified code will remain. The study team does not intend to retain data collected for this study for purposes not described in this application.

Table 2. Data and location of storage.

Data	**Location**
Subject intake	CHESS servers, Google Drive
Subject demographics	CHESS servers, Google Drive
Subject electronic consent	CHESS servers, Google Drive
De-identified Tula surveys	CHESS servers, Google Drive
De-identified Tula use data	CHESS servers, Google Drive
Interview data	HIP servers
Initial screening data	Qualtrics
Any other hardcopy records	Locked file cabinet

6.0 MEASUREMENT OF EFFECT

All scales have good psychometric properties with similar populations. Listed below are the factors to be measured and measurement instruments.

Intake only. Study staff will confirm patient eligibility via patients' UW Qualtrics screening surveys . Patients report demographics (biological sex, race, ethnicity, age, education).

Drinking and quality of life. Patients will be asked to take surveys administered via the Tula app (see Table 1 for frequencies). Patients will be asked to report on their drinking using the 7-day timeline follow-back[58,59] survey. Patients will also take the PROMIS Global Health[60] survey (10 items) to assess patient self-reported quality of life and a modified version of the Brief Alcohol Monitor[63] survey (10 items) to assess their risk and protection factors for problematic alcohol use. Alcohol use disorder severity (AUD scale,[64] 11 items; AUDIT, 10 items; 7-day timeline followback, 5 items) will be assessed at baseline and once every 3 months.

Mediators. Self-determination theory constructs will be assessed (see Table 1 for frequencies) via the Tula app as follows:

- Competence – Perceived Competence Scale (4 items)
- Relatedness – CHESS Bonding Scale[65,66] (5 items)
- Autonomous motivation – revised Treatment Self Regulations Questionnaire[67] (6 items)

Tula use. Tula use is collected in time-stamped log files and includes when a patient accessed Tula, the services used, duration of service use, pages viewed, messages posted and received, and content of messages. Tula use will be used to measure dose of intervention received for dose/response analyses. Patients will be asked to take a survey about their value of Tula at baseline and 12 months.

Healthcare utilization. Healthcare utilization will be collected from the self-reported medical services utilization form[61] (6 items; see Table 1 for frequency).

Intervention and implementation costs. Intervention costs will be determined using Tula time-stamped log files and billing codes logged by the health coach. Implementation costs will be determined through clinic staff interviews at the end of the intervention period. Cost per patient will be determined for each study group (self-monitored, peer-supported, and clinically integrated) with intervention and implementation costs separated within each group.

7.0 STUDY PARAMETERS

Patients will be block randomized by clinic, sex, and alcohol use severity to control for demographics at a 1:1:1 ratio to be in the self-monitoring, peer-supported Tula, or clinically integrated Tula groups. It's anticipated that 3-7 clinics (defined as having at least 10 patients in the study) with 3-7 clinicians each and 546 patient subjects will be recruited from the participating UW Health clinics. Patients will have access to Tula for up to 48 months, depending on time of enrollment, although the active period of participation is defined as 3 months with follow up through 12 months post enrollment (9 month follow-up). Health coaches will have access to patient-shared Tula data from patients of the clinically integrated Tula group for the duration of the study. The peer mentor will have access to discussion boards and private messages on Tula for the duration of the study for patients in the peer-supported

group. The research team will have access to all Tula data for all subjects in all groups for the duration of the study.

8.0 STATISTICAL CONSIDERATIONS

Analyses will assess the effectiveness between the three groups longitudinally on the primary and secondary outcomes.

Descriptive analyses. The research team will use descriptive statistics for all demographic and clinical variables across all three arms. To assess the impact of chance baseline imbalances between arms on intervention effect estimates, variables with noticeable differences will be included as covariates in a sensitivity analysis.

Intervention analyses. The analysis assesses direct treatment effects on patient outcomes over time over the 12-month study period. The research team will construct a longitudinal model of our outcome measures at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 months after randomization. The stratification variables will be by clinic, biological sex, and alcohol severity. They will be included as factors in the model and the baseline values of patient outcomes will be included as covariates, with a separate model for each primary outcome (risky drinking patterns , quality of life, and cost). This longitudinal analysis is complicated by the dependence among successive observations made on the same individual. Since complete control of measurement is not possible, there may be incomplete data from individual subjects. Therefore we will conduct a mixed-model analysis of repeated measures based on the general linear model with assessment of various covariance structures (compound symmetric, autoregressive order one, and unstructured). Covariance structure selection will be based on Akaike's information criterion and Schwarz's Bayesian criterion.[46, 47] Pairwise comparisons between treatment groups and specific treatment time contrasts in the mixed model will be conducted to respond to between-group effects and time-based effects. To address issues of incomplete data we plan to estimate treatment effects according to 4 approaches: intention-to-treat, as-treated, per-protocol, and complier-average causal effect. Missing data patters will be established from the longitudinal data and will be used to adjust the longitudinal intervention analysis according to pattern-mixture modeling.[69]

Mediation analysis. To augment the intervention analysis, we will estimate the effects that mediating variables have on the outcomes. Services in Tula were developed to meet three psychological needs (competence, relatedness, and autonomous motivation) and accordingly the research team will use a mediational model in which patients in the clinically integrated Tula group will improve these psychological needs, relative to the peer-supported Tula group and the self-monitoring group. In turn, the research team will analyze whether improvements in the psychological needs correlates to improved patient outcomes. Analyses will control for baseline scores on outcome variables and the design variables that are used to stratify our sample during randomization (site). The research team will use structural equation models to assess both direct and indirect influences of our intervention on patient outcomes.[70] To test the mediation effects via the 3 psychological needs, a mediation model

will be constructed to test the mediation effects between randomization variable and 12-month patient outcomes.

Operational cost analysis. Costs will be calculated based on tenets of engineering economics. This study will use incremental cost effectiveness ratios (ICERs) to quantify the tradeoff between the additional effectiveness achieved through clinical integration of the clinically integrated group compared to the peer-supported group. The main ICER will be the incremental cost per reduced drinking days over the 12-month period. We will train the health coach in the clinically integrated group to simulate use of CMS billing codes for mHealth to estimate potential reimbursement potential of the system that may be used to offset the costs of implementation.

Power. Power calculations are based on the previous randomized clinical trial of the platform.[71] The study is powered to detect a difference between groups in risky drinking episodes across the 12-month intervention period. Based on the attrition rate in the previous randomized clinical trial of Tula, we assume an attrition rate of 23% over the course of the study. To detect an effect size of Cohen's d=0.23 the research team will recruit 182 patients per group (546 patients total) to have sufficient power (1-β=0.8, multiple comparison adjusted α=0.0167, two-tailed). This would be a difference of 1.37 risky drinking episodes per month.

Quantitative data collection. The data collected in will come from multiple sources (see Table 1). Data collected from patient surveys will be collected by the Tula system and securely stored on CHESS servers. All log files will be stored on the CHESS server to be used to assess Tula use.

Qualitative data collection. This project will make use of clinician interviews to better understand the effect of Tula in the primary care setting. The interview will occur at intervention month 36 and take place at the clinicians' primary care clinic. Qualitative researchers will ask clinicians to talk about their experiences with Tula to refine the system for future use in primary care.

Qualitative data analysis. Content analysis will describe how Tula use can improve patient outcomes; identify potential improvements in Tula; and identify how qualitative data can supplement the quantitative analysis. A qualitative researcher will construct a coding scheme to assess the ideas of the study in order to capture references to a concept. The analyses will help the research team refine Tula for future dissemination by determining the individual and organizational conditions necessary to promote effectiveness.

9.0 BIBLIOGRAPHY

1. McKay JR, Van Horn DH, Oslin DW, Lynch KG, Ivey M, Ward K, et al. A randomized trial of extended telephone-based continuing care for alcohol dependence: within-treatment substance use outcomes. Journal of Consulting and Clinical Psychology. 2010;78(6):912-23.
2. Maisto SA, Zywiak WH, Connors GJ. Course of functioning 1 year following admission for treatment of alcohol use disorders. Addictive Behaviors. 2006;31(1):69-79.
3. Godley MD, Godley SH, Dennis ML, Funk R, Passetti LL. Preliminary outcomes from the assertive continuing care experiment for adolescents discharged from residential treatment. Journal of Substance Abuse Treatment. 2002;23(1):21-32.
4. Scherr D, Kastner P, Kollmann A, Hallas A, Auer J, Krappinger H, et al. Effect of home-based telemonitoring using mobile phone technology on the outcome of heart failure patients after an episode of acute decompensation: randomized controlled trial. Journal of Medical Internet Research. 2009;11(3):e34.
5. Noh JH, Cho YJ, Nam HW, Kim JH, Kim DJ, Yoo HS, et al. Web-based comprehensive information system for self-management of diabetes mellitus. Diabetes Technology & Therapeutics. 2010;12(5):333-7.
6. Helzer JE, Badger GJ, Rose GL, Mongeon JA, Searles JS. Decline in alcohol consumption during two years of daily reporting. Journal of Studies on Alcohol. 2002;63(5):551-8.
7. Davis JR, Glaros AG. Relapse prevention and smoking cessation. Addictive Behaviors. 1986;11(2):105-14.
8. Larimer ME, Palmer RS. Relapse prevention: An overview of Marlatt's cognitive-behavioral model. Alcohol Research & Health: The Journal of the National Institute on Alcohol Abuse and Alcoholism. 1999;23(2):151-60.
9. Seale JP, Shellenberger S, Velasquez MM, Boltri JM, Okosun I, Guyinn M, et al. Impact of vital signs screening & clinician prompting on alcohol and tobacco screening and intervention rates: a pre-post intervention comparison. BMC Family Practice. 2010;11:18.
10. Sullivan WP, Wolk JL, Hartmann DJ. Case management in alcohol and drug treatment: Improving client outcomes. Families in Society. 1992;73(10):195-204.
11. Dennis M, Scott CK, Funk R. An experimental evaluation of recovery management checkups (RMC) for people with chronic substance use disorders. Evaluation and Program Planning. 2003;26(3):339-52.
12. McLellan AT, Hagan TA, Levine M, Meyers K, Gould F, Bencivengo M, et al. Does clinical case management improve outpatient addiction treatment. Drug and Alcohol Dependence. 1999;55(1):91-13. Lorig KR, Ritter PL, Laurent DD, Fries JF. Long-term randomized controlled trials of tailored-print and small-group arthritis self-management interventions. Medical Care. 2004;42(4):346-54.
14. Rapp RC, Siegal HA, Fisher JH. A strengths-based model of case management/advocacy: adapting a mental health model to practice work with persons who have substance abuse problems. NIDA Research Monograph. 1992;127:79-91.
15. Shaw BR, Jeong Yeob H, Hawkins RP, McTavish FM, Gustafson DH. Communicating about self and others within an online support group for women with breast cancer and subsequent outcomes. Journal of Health Psychology. 2008;13(7):930-9.

16. Palermo TM, Wilson AC, Peters M, Lewandowski A, Somhegyi H. Randomized controlled trial of an Internet-delivered family cognitive-behavioral therapy intervention for children and adolescents with chronic pain. Pain. 2009;146(1-2)**:**205-13.
17. DuBenske LL, Gustafson DH, Shaw BR, Cleary JF. Web-based cancer communication and decision making systems: connecting patients, caregivers, and clinicians for improved health outcomes. Medical Decision Making : An International Journal of the Society for Medical Decision Making. 2010;30(6)**:**732-44.
18. Gustafson D, Wise M, Bhattacharya A, Pulvermacher A, Shanovich K, Phillips B, et al. The effects of combining Web-based eHealth with telephone nurse case management for pediatric asthma control: a randomized controlled trial. Journal of Medical Internet Research. 2012;14(4)**:**e101. PMCID: PMC3409549
19. Kim BY, Lee J. Smart devices for older adults managing chronic disease: a scoping review. JMIR mHealth and uHealth. 2017;5(5):e69.
20. Landro, L. How apps can help manage chronic diseases. The Wall Street Journal. 2017;
21. Logan AG, Irvine MJ, McIsaac WJ, Tisler A, Rossos PG, Easty A, et al. Effect of home blood pressure telemonitoring with self-care support on uncontrolled systolic hypertension in diabetics. Hypertension. 2012;60(1):51-7.
22. Artinian NT, Flack JM, Nordstrom CK, Hockman EM, Washington OG, Jen K-LC, et al. Effects of nurse managed telemonitoring on blood pressure at 12-month follow-up among urban African Americans. Nursing Research. 2007;56(5):312-22.
23. Green BB, Cook AJ, Ralston JD, Fishman PA, Catz SL, Carlson J, et al. Effectiveness of home blood pressure monitoring, Web communication, and pharmacist care on hypertension control: a randomized controlled trial. JAMA. 2008;299(24):2857-67.
24. Parati G, Omboni S, Albini F, Piantoni L, Giuliano A, Revera M, et al. Home blood pressure telemonitoring improves hypertension control in general practice. The TeleBPCare study. Journal of Hypertension. 2009;27(1):198-203.
25. Shea S, Weinstock RS, Starren J, Teresi J, Palmas W, Field L, et al. A randomized trial comparing telemedicine case management with usual care in older, ethnically diverse, medically underserved patients with diabetes mellitus. Journal of the American Medical Informatics Association. 2006;13(1):40-51.
26. Rinfret S, Lussier M-T, Peirce A, Duhamel F, Cossette S, Lalonde L, et al. The impact of a multidisciplinary information technology–supported program on blood pressure control in primary care. Circulation: Cardiovascular Quality and Outcomes 2009;2(3):170-7.
27. Rogers MA, Small D, Buchan DA, Butch CA, Stewart CM, Krenzer BE, et al. Home monitoring service improves mean arterial pressure in patients with essential hypertension: a randomized, controlled trial. Annals of Internal Medicine. 2001;134(11):1024-32.
28. McManus RJ, Mant J, Bray EP, Holder R, Jones MI, Greenfield S, et al. Telemonitoring and self-management in the control of hypertension (TASMINH2): a randomised controlled trial. The Lancet 2010;376(9736):163-72.
29. Parmanto B, Pramana G, Yu DX, Fairman AD, Dicianno BE, McCue MP. iMHere: a novel mhealth system for supporting self-care in management of complex and chronic conditions. JMIR mHealth and uHealth. 2013;1(2):e10.

30. Wisconsin Epidemiological Profile on Alcohol and Other Drug. Wisconsin Department of Health Services. Tables 27 to 30.; 2015. Accessed at: https://www.dhs.wisconsin.gov/publications/p4/p45718-16.pdf
31. Wisconsin Department of Health Services. Health Focus Area Profiles: Introduction and Mutual Influence of the Focus Areas. 2015; 15. Accessed at: https://www.dhs.wisconsin.gov/publications/p0/p00816-health-profiles.pdf
32. Esser MB, Hedden SL, Kanny D, Brewer RD, Gfroerer JC, Naimi TS. Prevalance of Alcohol Dependence Among US Adult Drinkers. US National Library of Medicine. 2009-2011;11.
33. Grant S, Watkins KE, Bogart A, Paddock SM, Hepner KA. Patient-Reported Offers of Alcohol Treatment for Primary Care Patients at High-Risk for an Alcohol Use Disorder. Journal of the American Board of Family Medicine. 2016;29(6):682-87.
34. Bradizza CM, Stasiewicz PR, Paas ND. Relapse to alcohol and drug use among individuals diagnosed with co-occurring mental health and substance use disorders: a review. Clinical Psychology Review 2006;26(2):162-78.
35. Brownell KD, Marlatt GA, Lichtenstein E, Wilson GT. Understanding and preventing relapse. The American Psychologist 1986;41(7):765-82.
36. Donovan DM. Assessment issues and domains in the prediction of relapse. Addiction 1996;91(12s1):2936.
37. Lowman C, Allen J, Stout RL, Group TRR. Replication and extension of Marlatt's taxonomy of relapse precipitants: overview of procedures and results. Addiction. 1996;91(12s1):51-72.
38. McKay JR, Weiss RV. A review of temporal effects and outcome predictors in substance abuse treatment studies with long-term follow-ups preliminary results and methodological issues. Evaluation Review 2001;25(2):113-61.
39. McLellan A. The outcomes movement in substance abuse treatment: comments, concerns and criticisms. In: Sorenson JL, Rawson RA, Guydish A, Zweben JE, eds. Drug abuse treatment through collaboration: practice and research partnerships that work. Washington, DC: American Psychological Association; 2002: 119-34.
40. Mueller S, Petitjean S, Boening J, Wiesbeck G. The impact of self-help group attendance on relapse rates after alcohol detoxification in a controlled study. Alcohol and Alcoholism 2007;42(2):108-12.
41. Witkiewitz K, Marlatt GA. Relapse prevention for alcohol and drug problems: that was Zen, this is Tao. American Psychologist. 2004;59(4):224.
42. Marlatt GA, Witkiewitz K. Relapse prevention for alcohol and drug problems. Relapse prevention: maintenance strategies in the treatment of addictive behaviors. Guilford Press. 2005.
43. Gustafson DH, Hawkins R, Boberg E, Pingree S, Serlin RE, Graziano F, et al. Impact of a patient-centered, computer-based health information/support system. American Journal of Preventive Medicine. 1999;16(1):1-9.

44. Gustafson DH, Hawkins R, McTavish F, Pingree S, Chen WC, Volrathongchai K, et al. Internet-based interactive support for cancer patients: are integrated systems better? The Journal of Communication. 2008;58(2)**:**238-57.
45. Sklar SM, Turner NE. A brief measure for the assessment of coping self-efficacy among alcohol and other drug users. Addiction. 1999;94(5):723-9.
46. Akaike H. A new look at the statistical model identification. Automatic Control, IEEE Transactions on Automatic Control. 1974;19(6):716-23.
47. Schwarz G. Estimating the dimension of a model. The Annals of Statistics. 1978;6(2):461-4.
48. Little RJ, Yau LHY. Statistical techniques for analyzing data from prevention trials: treatment of no-shows using Rubin's causal model. Psychological Methods. 1998;3(2):147.
49. Jo B. Statistical power in randomized intervention studies with noncompliance. Psychological Methods. 2002;7(2):178.
50. Thoits PA. Stress, coping, and social support processes: Where are we? What next? Journal of Health and Social Behavior. 1995:53-79.
51. Quanbeck A, Gustafson DH, Marsch LA, Chih MY,Kornfield R, McTavish F, et al. Implementing a Mobile Health System to Integrate the Treatment of Addiction Into Primary Care: A Hybrid Implementation-Effectiveness Study. Journal of Medical Internet Research. 2018;20(1):e37.
52. Cella DF, Sarafian B, Snider PR, Yellen SB, Winicour P. Evaluation of a community-based cancer support group. Psycho-Oncology. 1993;2(2):123-32.
53. Krizek C, Roberts C, Ragan R, Ferrara JJ, Lord B. Gender and cancer support group participation. Cancer Practice. 1999;7(2):86-92.
54. Van Uden-Kraan CF, Drossaert CH, Taal E, Seydel ER, van de Laar MA. Participation in online patient support groups endorses patients' empowerment. Patient Education and Counseling. 2009;74(1):61-9.
55. Van Uden-Kraan CF, Drossaert CH, Taal E, Smit WM, Bernelot Moens HJ, Van de Laar MA. Determinants of engagement in face-to-face and online patient support groups. Journal of Medical Internet Research. 2011;13(4):e106.
56. Namkoong K, McLaughlin B, Yoo W, Hull SJ, Shah DV, Kim SC, et al. The effects of expression: how providing emotional support online improves cancer patients' coping strategies. Journal of the National Cancer Institute. Monographs. 2013;2013(47):169-74.
57. Yoo W, Namkoong K, Choi M, Shah DV, Tsang S, Hong Y, et al. Giving and receiving emotional support online: communication competence as a moderator of psychosocial benefits for women with breast cancer. Computers in Human Behavior 2014;30:13-22.
58. Sacks JAY, Drake RE, Williams VF, Banks SM, Herrell JM. Utility of the Time-Line Follow-Back to assess substance use among homeless adults. The Journal of Nervous and Mental Disease. 2003;191(3):145-53.

59. Fals-Stewart W, O'Farrell TJ, Freitas TT, McFarlin SK, Rutigliano P. The timeline followback reports of psychoactive substance use by drug-abusing patients: psychometric properties. Journal of Consulting and Clinical Psychology. 2000;68(1):134.
60. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. Quality of Life Research. 2009;18(7):873-80.
61. Polsky D, Glick HA, Yang J, Subramaniam GA, Poole SA, Woody GE. Cost-effectiveness of extended buprenorphine-naloxone treatment for opioid-dependent youth: data from a randomized trial. Addiction. 2010;105(9):1616-24.
62. Saldana L, Chamberlain P, Bradford WD, Campbell M, Lansverk J. The cost of implementing new strategies (COINS): a method for mapping implementation resources using the Stages of Implementation Completion. Children and Youth Services Review. 2014;39,177-182.
63. Cacciola JS, Alterman AI, DePhilippis D, Drapkin ML, Valadez C, Jr., Fala NC, et al. Development and initial evaluation of the Brief Addiction Monitor (BAM). Journal of Substance Abuse Treatment. 2013;44(3):256-63.
64. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Alcohol Use Disorder: A Comparison Between DSM-IV and DSM-5. NIH, National Institute on Alcohol Abuse and Alcoholism; 2016.
65. Namkoong K, DuBenske LL, Shaw BR, Gustafson DH, Hawkins RP, Shah DV, et al. Creating a bond between caregivers online: effect on caregivers' coping strategies. Journal of Health Communication. 2012;17(2):125-40.
66. Williams GC, Cox EM, Kouides R, Deci EL. Presenting the facts about smoking to adolescents: effects of an autonomy-supportive style. Archives of Pediatrics & Adolescent Medicine. 1999;153(9):959-64.
67. Eagly AH, Crowley M. Gender and helping behavior: a meta-analytic review of the social psychological literature. Psychological Bulletin. 1986;100(3):283.
68. Hyde JS. Gender similarities and differences. Annual Review of Psychology. 2014;65:373-98.
69. Hedeker D, Gibbons RD, Waternaux C. Sample size estimation for longitudinal designs with attrition: comparing time-related contrasts between two groups. Journal of Educational and Behavioral Statistics. 1999;24(1):70-93.
70. Short LM, Hennessy M. Using structural equations to estimate effects of behavioral interventions. Structural Equation Modeling: A Multidisciplinary Journal. 1994;1(1):68-81.
71. Gustafson DH, McTavish FM, Chih MY, Atwood AK, Johnson RA, Boyle MG, et al. A smartphone application to support recovery from alcoholism: a randomized clinical trial. JAMA Psychiatry. 2014;71(5):566-72.